

**APPENDIX II**  
**CLEAN VERSION OF THE ENTIRE SET OF PENDING CLAIMS**

1. (Once Amended) A method of reducing or inhibiting angiogenesis in a tissue, comprising contacting  $\alpha 5\beta 1$  integrin in the tissue with an  $\alpha 5\beta 1$  antagonist that interferes with specific binding of the  $\alpha 5\beta 1$  integrin to a ligand expressed in the tissue, thereby reducing or inhibiting angiogenesis in the tissue.

2. (Once Amended) The method of claim 1, wherein the antagonist does not substantially interfere with the specific binding of a ligand to an integrin other than  $\alpha 5\beta 1$  integrin to its ligand.

3. The method of claim 1, wherein the ligand is fibronectin.

4. The method of claim 1, wherein the tissue comprises ocular tissue.

5. The method of claim 4, wherein the ocular tissue is selected from the group consisting of retina, macula and cornea.

9. The method of claim 1, wherein the tissue comprises a neoplasm.

10. The method of claim 9, wherein the neoplasm is a malignant neoplasm.

11. The method of claim 10, wherein the malignant neoplasm is a metastatic malignant neoplasm.

12. The method of claim 10, wherein the malignant neoplasm is a carcinoma.

13. (Once Amended) The method of claim 1, wherein the antagonist comprises a peptide.

14. The method of claim 13, wherein the peptide comprises the amino acid sequence CRRETAWAC (SEQ ID NO: 1).

19. (Once Amended) The method of claim 1, wherein the antagonist is linked to a cytotoxin.

20. The method of claim 19, wherein the cytotoxin is a cancer chemotherapeutic drug.

55. (Once Amended) A method of reducing or inhibiting angiogenesis in a tissue in an individual, comprising administering to the individual an  $\alpha 5\beta 1$  antagonist that interferes with the specific binding of  $\alpha 5\beta 1$  integrin to a ligand expressed in the tissue, thereby reducing or inhibiting angiogenesis in the tissue in the individual.

56. The method of claim 55, wherein the individual is a human.
57. (Once Amended) A method of reducing the severity of a pathological condition associated with angiogenesis in an individual, comprising administering to the individual an  $\alpha 5\beta 1$  antagonist that interferes with specific binding of  $\alpha 5\beta 1$  integrin to a ligand in a tissue associated with the pathological condition, thereby reducing or inhibiting angiogenesis in the tissue, and reducing the severity of the pathological condition.
58. The method of claim 57, wherein the pathological condition is a neoplasm.
59. The method of claim 58, wherein the neoplasm is a malignant neoplasm.
60. The method of claim 59, wherein the malignant neoplasm is a metastatic malignant neoplasm.
61. The method of claim 59, wherein the malignant neoplasm is a carcinoma.
62. The method of claim 61, wherein the carcinoma is selected from the group consisting of a breast carcinoma, a colon carcinoma, an ovarian carcinoma and a pancreatic carcinoma.
63. The method of claim 59, wherein the malignant neoplasm is selected from the group consisting of a sarcoma, a mesothelioma, a teratocarcinoma, an astrocytoma, and a glioblastoma.
64. The method of claim 57, wherein the individual is a human.
65. (Once Amended) The method of claim 57, wherein the antagonist is administered intravenously.
66. (Once Amended) The method of claim 57, wherein the antagonist is administered orally.
67. (Once Amended) The method of claim 58, wherein the antagonist is administered into a neoplasm.
68. The method of claim 57, wherein the pathological condition is associated with the eye.
69. The method of claim 68, wherein the pathological condition is selected from the group consisting of diabetic retinopathy and macular degeneration by neovascularization.
70. (Once Amended) The method of claim 68, wherein the antagonist is administered in the form of eye drops.

71. (Once Amended) The method of claim 68, wherein the antagonist is administered intravenously.

72. (Once Amended) The method of claim 68, wherein the antagonist is administered orally.

75. (Once Amended) The method of claim 57, wherein the antagonist is administered at a dose of 0.0001 to 100 mg/kg body weight.

80. (Once Amended) The method of Claim 1, wherein the binding of said antagonist to said  $\alpha 5\beta 1$  integrin is at least two-fold greater than the binding of said antagonist to an integrin other than  $\alpha 5\beta 1$  integrin.

81. The method of Claim 80, wherein said integrin other than  $\alpha 5\beta 1$  integrin is  $\alpha V\beta 3$  integrin.

82. (Once Amended) The method of Claim 1, wherein the binding of said antagonist to said  $\alpha 5\beta 1$  integrin is at least five-fold greater than the binding of said antagonist to an integrin other than  $\alpha 5\beta 1$  integrin.

83. The method of Claim 82, wherein said integrin other than  $\alpha 5\beta 1$  integrin is  $\alpha V\beta 3$  integrin.

84. (Once Amended) The method of Claim 1, wherein the binding of said antagonist to said  $\alpha 5\beta 1$  integrin is at least ten-fold greater than the binding of said antagonist to an integrin other than  $\alpha 5\beta 1$  integrin.

85. The method of Claim 84, wherein said integrin other than  $\alpha 5\beta 1$  integrin is  $\alpha V\beta 3$  integrin.

86. (Once Amended) The method of Claim 1, wherein said antagonist does not interfere with the specific binding of a ligand to an integrin other than  $\alpha 5\beta 1$  integrin.

87. The method of Claim 1, wherein said tissue is in a human subject.

88. The method of Claim 10, wherein said malignant neoplasm is selected from the group consisting of a sarcoma, a mesothelioma, a teratocarcinoma, an astrocytoma, and a glioblastoma.

89. The method of Claim 12, wherein said carcinoma is selected from the group consisting of a breast carcinoma, a colon carcinoma, an ovarian carcinoma and a pancreatic carcinoma.

90. (Once Amended) The method of Claim 55, wherein the binding of said antagonist to said  $\alpha 5\beta 1$  integrin is at least two-fold greater than the binding of said antagonist to an integrin other than  $\alpha 5\beta 1$  integrin.

91. The method of Claim 90, wherein said integrin other than  $\alpha 5\beta 1$  integrin is  $\alpha V\beta 3$  integrin.

92. (Once Amended) The method of Claim 55, wherein the binding of said antagonist to said  $\alpha 5\beta 1$  integrin is at least five-fold greater than the binding of said antagonist to an integrin other than  $\alpha 5\beta 1$  integrin.

93. The method of Claim 92, wherein said integrin other than  $\alpha 5\beta 1$  integrin is  $\alpha V\beta 3$  integrin.

94. (Once Amended) The method of Claim 55, wherein the binding of said antagonist to said  $\alpha 5\beta 1$  integrin is at least ten-fold greater than the binding of said antagonist to an integrin other than  $\alpha 5\beta 1$  integrin.

95. The method of Claim 94, wherein said integrin other than  $\alpha 5\beta 1$  integrin is  $\alpha V\beta 3$  integrin.

96. (Once Amended) The method of Claim 55, wherein said antagonist does not interfere with the specific binding of a ligand to an integrin other than  $\alpha 5\beta 1$  integrin.

97. The method of Claim 55, wherein said ligand is fibronectin.

98. The method of Claim 55, wherein said tissue comprises ocular tissue.

99. The method of Claim 98, wherein said ocular tissue is selected from the group consisting of retina, macula and cornea.

100. The method of Claim 55, wherein said tissue comprises a neoplasm.

101. The method of Claim 100, wherein said neoplasm is a malignant neoplasm.

102. The method of Claim 101, wherein said malignant neoplasm is selected from the group consisting of a sarcoma, a mesothelioma, a teratocarcinoma, an astrocytoma, and a glioblastoma.

103. The method of Claim 101, wherein said malignant neoplasm is a metastatic malignant neoplasm.

104. The method of Claim 101, wherein said malignant neoplasm is a carcinoma.

105. The method of Claim 104, wherein said carcinoma is selected from the group consisting of a breast carcinoma, a colon carcinoma, an ovarian carcinoma and a pancreatic carcinoma.

106. (Once Amended) The method of Claim 55, wherein said antagonist comprises a peptide.

107. The method of Claim 106, wherein said peptide comprises the amino acid sequence CRRETAWAC (SEQ ID NO: 1).

108. (Once Amended) The method of Claim 55, wherein said antagonist is linked to a cytotoxin.

109. The method of Claim 108, wherein said cytotoxin is a cancer chemotherapeutic drug.

110. (Once Amended) The method of Claim 57, wherein the binding of said antagonist to said  $\alpha 5\beta 1$  integrin is at least two-fold greater than the binding of said antagonist to an integrin other than  $\alpha 5\beta 1$  integrin.

111. The method of Claim 110, wherein said integrin other than  $\alpha 5\beta 1$  integrin is  $\alpha V\beta 3$  integrin.

112. (Once Amended) The method of Claim 57, wherein the binding of said antagonist to said  $\alpha 5\beta 1$  integrin is at least five-fold greater than the binding of said antagonist to an integrin other than  $\alpha 5\beta 1$  integrin.

113. The method of Claim 112, wherein said integrin other than  $\alpha 5\beta 1$  integrin is  $\alpha V\beta 3$  integrin.

114. (Once Amended) The method of Claim 57, wherein the binding of said antagonist to said  $\alpha 5\beta 1$  integrin is at least ten-fold greater than the binding of said antagonist to an integrin other than  $\alpha 5\beta 1$  integrin.

115. The method of Claim 114, wherein said integrin other than  $\alpha 5\beta 1$  integrin is  $\alpha V\beta 3$  integrin.

116. (Once Amended) The method of Claim 57, wherein said antagonist does not interfere with the specific binding of a ligand to an integrin other than  $\alpha 5\beta 1$  integrin.

117. (Once Amended) The method of Claim 57, wherein said antagonist comprises a peptide.

118. The method of Claim 117, wherein said peptide comprises the amino acid sequence CRRETAWAC (SEQ ID NO: 1).

119. (Once Amended) The method of Claim 57, wherein said antagonist is linked to a cytotoxin.

120. The method of Claim 119, wherein said cytotoxin is a cancer chemotherapeutic drug.

121. (New) A method of reducing or inhibiting angiogenesis in a tissue, comprising contacting  $\alpha 5\beta 1$  integrin in the tissue with an  $\alpha 5\beta 1$  antagonist that induces endothelial cell apoptosis and interferes with specific binding of the  $\alpha 5\beta 1$  integrin to a ligand expressed in the tissue, thereby reducing or inhibiting angiogenesis in the tissue. = 51

122. (New) A method of reducing or inhibiting angiogenesis in a tissue in an individual, comprising administering to the individual an  $\alpha 5\beta 1$  antagonist that induces endothelial cell apoptosis and interferes with the specific binding of  $\alpha 5\beta 1$  integrin to a ligand expressed in the tissue, thereby reducing or inhibiting angiogenesis in the tissue in the individual. = 55

123. (New) A method of reducing the severity of a pathological condition associated with angiogenesis in an individual, comprising administering to the individual an  $\alpha 5\beta 1$  antagonist that induces endothelial cell apoptosis and interferes with specific binding of  $\alpha 5\beta 1$  integrin to a ligand in a tissue associated with the pathological condition, thereby reducing or inhibiting angiogenesis in the tissue, and reducing the severity of the pathological condition. = 57